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EXAMINER
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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/052,931	NOUADJE ET AL.	
	Examiner	Art Unit	
	Alan Diamond	1753	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5,7-25,27-30 and 33-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,5,7-25,27-30 and 33-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Comments

1. The objection to the specification has been overcome by Applicant's amendment thereof.

2. The objection to claims 1, 8, 9, 19, and 24 for informalities has been overcome by Applicant's amendment of the claims.

3. The rejection of claims 25, 29, 30 and 33 under 35 USC 112, second paragraph, has been overcome by Applicant's amendment of claim 25.

4. The rejection of independent claim 24 and its dependent claims over Lauer et al has been overcome by Applicant's amendment of claim 24 so as to require that that the C_6 to C_{22} alkyl-mono, di-, or tri-sulfonates are linear alkyl. None of the sulfonic acid buffers listed in Lauer et al's Table II are linear C_6 to C_{22} alkyl mono, di- or tri-sulphonates.

5. The rejection of claim 24 and its dependent claims over Keo et al has been overcome by Applicant's amendment of claim 24 so as to require that that the C_6 to C_{22} alkyl-mono, di-, or tri-sulfonates are linear alkyl. The CAPS buffer used by Keo et al does not read on or render obvious the additive as now claimed in claim 24.

6. The rejection of claim 24 and its dependent claims over Alter et al has been overcome by Applicant's amendment of claim 24 so as to require that that the C_6 to C_{22} alkyl-mono, di-, or tri-sulfonates are linear alkyl. The TES buffer used by Keo et al does not read on or render obvious the additive as now claimed in claim 24, and, as argued

by Applicant at the bottom of page 13 of the Remarks filed 10/31/2005, TES could not have a hydrophobic interaction with human albumin.

7. The rejection of claims 25 (and its dependent claims 29 and 33) using Ogawa et al has been overcome by Applicant's amendment of claim 25 so as to require that that the C_6 to C_{22} alkyl-mono, di-, or tri-sulfonates are linear alkyl. Likewise, claim 29 now requires that the additive is a linear C_6 to C_{10} alkylsulphonate. The TAPS buffer used by Ogawa et al is C_7 alkylsulphonate, but not linear.

Claim Objections

8. Claim 33 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 33 does not further limit claim 25 because a linear C_6 to C_{22} alkyl-mono-, di-, or tri-sulphonate is not a zwitterionic buffer.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claim 33 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had

possession of the claimed invention. In claim 33, an additive that is linear C_6 to C_{22} alkyl-mono-, di-, or tri-sulphonates and also a zwitterionic biological buffer is not supported by the specification, as originally filed.

11. Claim 33 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification is not enabling for an additive that is linear C_6 to C_{22} alkyl-mono-, di-, or tri-sulphonates and also a zwitterionic biological buffer.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 24, 25, 27-30 and 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 20 is now indefinite because it recites a method for separating at least one protein constituent in a human biological sample, yet the only thing that is passed into the capillary is the at least on protein constituent. It is not clear what the at least one protein constituent is separated from if it is the only thing that is positively recited as being passed into the capillary.

Claim 24 is now indefinite because it is not clear exactly what the solution comprises. It is not clear what is meant by "in a liquid support and at least one buffer and additive" at lines 2-3. The same applies to dependent claims 25, 27-30, and 33.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. Claims 1, 2, 5, 7-10, 12-21, 23, and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lauer et al, "Capillary Zone Electrophoresis of Proteins in Untreated Fused Silica Tubing," Anal. Chem., Vol. 58, pages 166-170, (1986) in view of Karger et al (U.S. Patent 4,778,909).

With respect to independent claims 1, 20, and 21 Lauer et al teaches a buffer system in water for capillary zone electrophoresis of a protein mixture, wherein the buffer system comprises, at pH 9.22, 20 mM CHES buffer, i.e., (cyclohexylamino)ethanesufonic acid buffer, which reads on both the instant buffer and the instant additive (i.e., reads on the instant C_6 to C_{22} alkyl-monosulfonate additive and C_6-C_{10}-alkylsulphonate) (see the experimental section at page 167; and Figure 2 at page 168). The buffer system further contains KCl (see Figure 2 at page 168). The CHES buffer used by Lauer et al (see Figure 2) during its capillary zone electrophoresis has an anionic pole (from the sulfonic acid group) with a pH of more than 9 and a hydrophobic portion, from the (cyclohexylamino)ethane group. Indeed, CHES is mentioned on page 6, line 19, of the instant specification as an example of the instant additive. The proteins selected by Lauer et al were those that covered a wide range of isoelectric points and molecular weight (see page 167).

With respect to claims 7 and 8, and as noted above, CHES has an anionic pole (from the sulfonic acid group) and a hydrophobic portion, from the (cyclohexylamino)ethane group.

With respect to claims 9 and 10, and as also noted above, CHES reads on the instant C_6 to C_{22} alkyl-monosulfonate additive. CHES is a C_8 alkylsulfonate.

With respect to claims 12 and 13, the CHES has a concentration of 20 mM (see Figure 2 at page 168). It is the Examiner's position that the 20 mM CHES does not exceed the critical micellar concentration of the CHES.

With respect to claim 16, the pH is 9.22 (see Figure 2 at page 168).

With respect to claim 17, the capillary tube is fused silica (see the title, abstract, and the experimental section at page 167).

With respect to claims 18 and 19, NaOH or HCl is used for adjusting pH (see the paragraph bridging the left and right column on page 167).

With respect to claim 23, said CHES is a zwitterionic biological buffer.

Lauer et al teaches the limitations of the instant claims other than the difference which is discussed below.

None of the proteins tested in Table I at page 167 of Lauer et al is a serum protein. Karger et al is relied upon for showing that human transferrin (i.e., human β_1-globulin), which is a serum protein, has a pI of 5.0 and a molecular weight of 77,000 (see Table VIII at col. 19). It would have been obvious to one of ordinary skill in the art at the time the invention was made to have used human transferrin in Lauer et al's capillary zone electrophoresis because this protein has a pI value (as shown by Karger

et al) within the range of pI values set forth in Table I of Lauer et al. While it is true that said human transferrin has a higher molecular weight than many of those in Lauer et al's Table I, it should be noted that Lauer et al is not limited to the protein molecular weights in said Table I. In any event, Conalbumin listed in Lauer et al's Table I also has a molecular weight of 77,000. Said human transferrin renders obvious the instant human biological sample. With respect to claim 2, when the human transferrin is separated from the other model proteins used by the capillary zone electrophoresis, the instant protein constituent will have been separated. Since the CHES buffer is the same as the instant additive, it will hydrophobically interact with the human transferrin, as in claim 1, and would have a hydrophobic interaction with human albumin as in claim 20.

With respect to claims 14 and 15, Lauer et al does not specifically teach that its CHES buffer concentration can be 1 mM to 4 mM, e.g., about 2.5 mM, instead of the 20 mM that is used in Figure 2 at page 168. However, Lauer et al is not limited to the 20 mM. Any concentration of CHES buffer that would provide buffering is within its purview. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have used a lower concentration of the CHES buffer, i.e., to have used a CHES buffer concentration of, for example 4 mM or 2.5 mM, to perform Lauer et al's capillary zone electrophoresis because Lauer et al is not limited to the 20 mM, and any concentration of CHES buffer that would provide buffering, such as 4 mM or 2.5 mM is within its purview.

16. Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lauer et al in view of Karger et al as applied to claims 1, 2, 5, 7-10, 12-21, 23, and 34 above, and further in view of Ohmura et al, U.S. Patent 5,521,287.

Lauer et al in view of Karger et al, as relied upon for the reasons recited above, teaches the limitations of claim 22, the difference being that Lauer et al et al does not specifically teach the use of sodium sulfate in place of said KCl. Ohmura et al teaches that salts for adjusting ionic strength include KCl and sodium sulfate (see the paragraph bridging cols. 7 and 8). It would have been obvious to one of ordinary skill in the art at the time the invention was made to have substituted the KCl in Lauer et al's buffer with sodium sulfate because the substitution of art recognized equivalent salts for adjusting ionic strength, as shown by Ohmura et al, would have been within the skill of an artisan.

17. Claims 1, 4, 5, 7-10, 12-21, 23, and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keo et al, U.S. Patent 5,599,433.

With respect to claims 1, 20, 21, and 23 Keo et al teaches the capillary zone electrophoresis (CZE) of glycosylated proteins in clinical specimens, wherein the buffer system is a solution that contains, for example, 100 mM CAPS, i.e., 3-cyclohecylamino-1-propanesulfonic acid (which reads on the instant zwitterionic biological buffer and additive), 300 mM sodium borate (which is a buffer), and NaOH for adjusting the pH to 11 (see col. 3, lines 32-55; col. 4, lines 43-49; col. 5, line 16 through col. 6, line 14; and col. 8, lines 32-43). It should be noted that CAPS is C_9 alkylsulfonate. Alternatively, the pH can be at 10 (see col. 10, line 46). It is noted that the instant specification teaches, at page 6, lines 17-20, that CAPS is an instant additive. The water in Keo et al's buffer

system reads on the support in claim 24. The clinical specimen can be a human biological liquid such as serum, plasma, cerebrospinal fluid, urine, etc (see col. 6, lines 17-22). These biological liquids, and in particular, the serum and plasma, inherently contain the instant albumin, α_1-globulin, α_2-globulin, β-globulin, β_1-globulin, β_2-globulin, and γ-globulin. It is the Examiner's position that said CAPS buffer has a hydrophobic interaction with the albumin, α_1-globulin, α_2-globulin, β-globulin, β_1-globulin, β_2-globulin, and γ-globulin and provides these proteins with at least one negative charge thereby modifying the electrophorectic mobility.

With respect to claim 4, said serum, plasma, cerebrospinal fluid, or urine, etc, is a biological sample (see col. 6, lines 17-22).

With respect to claim 5, said albumin, α_1-globulin, α_2-globulin, β-globulin, β_1-globulin, β_2-globulin, and γ-globulin, in said serum or plasma, is a blood protein.

With respect to claims 7-10, said CAPS, which is a C_9 alkylsulfonate, has an anionic pole with a pH of more than 9 and a hydrophobic portion.

With respect to claim 12, the CAPS is present at a concentration of, example, 100 mM (see col. 6, lines 12-13), and it is the Examiner's position that this concentration does not exceed the critical micellar concentration of the CAPS.

With respect to claim 16, the pH can be 10 or 11 (see col. 6, line 14; and col. 10, line 46).

With respect to claim 17, a fused silica capillary tube is used (see col. 8, lines 21-22).

With respect to claims 18 and 19, and as noted above, the buffer contains NaOH for adjusting the pH (see col. 6, lines 13-14).

Keo et al teaches the limitations of the instant claims other than the differences which are discussed below.

With respect to claims 14 and 15, Keo et al does not specifically teach that its CAPS buffer concentration can be 1 mM to 4 mM, e.g., about 2.5 mM. Keo et al teaches that the CAPS buffer can be present at a concentration of about 10 mM to about 200 mM (see col. 6, lines 9-10). It is the Examiner's position that going slightly lower than the 10 mM concentration would have been within the skill of an artisan. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have used a lower concentration of Keo et al's CAPS buffer, below the 10 mM concentration sated by Keo et al, i.e., to have used a CAPS buffer concentration of, for example 4 mM or 2.5 mM, to perform Keo et al's capillary zone electrophoresis, because the use of slightly lower concentrations of buffer would have been within the level of ordinary skill in the art.

Keo et al does not specifically require that said buffer system containing the CAPS, sodium borate, and NaOH be used for the serum, plasma, cerebrospinal fluid, or urine biological fluid. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used said buffer system containing CAPS, sodium borate, and NaOH for the serum, plasma, cerebrospinal fluid, or urine biological fluid because such is clearly within the scope of Keo et al's disclosure.

18. Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ogawa et al, U.S. Patent 4,769,408.

Ogawa et al prepares an aqueous solution comprising buffer and an anionic surfactant such as sodium dodecylsulfate (see col. 13, line 22 through col. 14, line 64; and Example 1 at cols. 15-16). Sodium dodecylsulfate, which is a C_{12} alkylsulfate, reads on the instant additive. The pH of the solution can be, for example, 10 (se col. 13, lines 41-42). The water in the solution reads on the instant liquid support. The recitation "for capillary electrophoresis" is merely intended use and is not deemed to be a positive limitation of the instant claims. Ogawa et al teaches the limitations of the instant claim other than the difference which is discussed below.

Ogawa et al does not specifically prepare its solution having a pH of 10 with said sodium dodecylsulfate. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have prepared Ogawa et al's solution having a pH of 10 with sodium dodecylsulfate because such is clearly within the scope of Ogawa et al's disclosure.

19. Claims 24, 25, and 27-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bellon et al (U.S. Patent 5,928,484) in view of Keyes (U.S. Patent 4,714,677) and Bloebaum et al (U.S. Patent 4,872,865).

Bellon et al teaches a buffer solution comprising Tris buffer and 1-hydroxy naphthalene 2-carboxylic acid (which reads on the instant additive) (see Example IV at col. 11). In place of said 1-hydroxy naphthalene 2-carboxylic acid, there can be used sodium cholate, sodium dodecylbenzenesulfonate, sodium dodecylsulfate, naphthalene

2-carboxylic acid, or naphthalene 2-sulfonic acid (which each read on the instant additive) (see col. 6, lines 10-55). Said 1-hydroxy naphthalene 2-carboxylic acid, sodium cholate, sodium dodecylbenzenesulfonate, sodium dodecylsulfate, naphthalene 2-carboxylic acid, and naphthalene 2-sulfonic acid are examples of Bellon et al's molecules that have a hydrophobic moiety (see col. 6, lines 10-55). In general, said molecule having a hydrophobic moiety can, for example, comprise a linear or branched aliphatic chain of 3 to 10 carbon atoms bearing a sulfonic acid function. It is the Examiner's position that this encompasses C_6 to C_{10} alkyl sulfonates, such as octanesulfonate. The pH can be at about 9, and it is the Examiner's position that said Tris buffer can buffer at a pH of about 9 (see col. 5, line 43). Bellon et al teaches the limitations of the instant claims other than the difference which is discussed below.

Bellon et al does not specifically require a pH of between 9 and 11 for its buffer solution, i.e., in Bellon et al's examples (see cols. 10 to 11) the pH is never given. However, as noted above, Bellon et al uses Tris buffer, and the pH can be about 9. Furthermore, Keyes (col. 17, lines 39-40 and 49) and Bloebaum et al (col. 6, line 33) are relied upon for showing that Tris can buffer at pH 9.1. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have prepared Bellon et al's buffer solution at a pH of about 9, such as 9.1 because Tris can buffer at such a pH, as shown by Keyes and Bloebaum et al, and Bellon et al teaches a pH of about 9, as noted above.

Bellon et al does not specifically teach that its molecule having a hydrophobic moiety can be a C_6 to C_{10} alkyl sulfonates, such as octanesulfonate. However, it would

have been obvious to one of ordinary skill in the art at the time the invention was made to have used a C_6 to C_{10} alkyl sulfonates, such as octanesulfonate for Bellon et al's molecule having a hydrophobic moiety because Bellon et al teaches that its molecule having a hydrophobic moiety can comprise a linear or branched aliphatic chain of 3 to 10 carbon atoms bearing a sulfonic acid function.

Double Patenting

20. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

21. Claims 1, 2, 4, 5, 7-25, 27-30, and 33-35 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 8-28, and 30 of copending Application No. 10/052,601. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method claims in said copending application are anticipatory of the instant method claims, but are of a different scope. For example, claim 20 in said copending application teaches the use of octanesulphonate as an additive in the buffer for capillary electrophoresis. Claim 21 in said copending application teaches a concentration of 1 to

5 mM. Note that claim 1 in said copending application analyzes the same proteins as in instant claim 1. The biological buffer in claim 1 of said patent, such as CAPS, also reads on the instant additive. CAPS is a C_9 alkylsulfonate. When one prepares the buffer system in the method claims of said copending application, the instant solution will be obtained.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

22. Applicant's arguments filed October 31, 2005 have been fully considered but they are not persuasive.

Applicant argues that Lauer et al's proteins appear to be exclusively of a non-human origin, and that the process disclosed in Lauer et al "cannot be understood as a process according the invention where materials of separated and analyzed from human samples of a biological origin." However, this argument is not deemed to be persuasive because the process for analyzing in instant claim 1 recites a process step of "introducing" the sample into a capillary tube. Lauer et al introduces its protein mixture into a capillary tube so as to perform capillary zone electrophoresis (see the entire document). Instant claim 2 does recite a step of "separating said at least one protein constituent by migrating and detecting said at least one protein constituent." However, Lauer et al separates its protein constituents by migrating and detecting, as evidenced by the electgropherograms in Lauer et al's Figures 1, 2, and 3. Instant claim 1 now requires that the sample is a human biological sample. However, as noted

above, Karger et al is relied upon for showing that human transferrin i.e., human β_1-globulin, which is a serum protein, has a pI of 5.0 and a molecular weight of 77,000 (see Table VIII at col. 19). It would have been obvious to one of ordinary skill in the art at the time the invention was made to have used human transferrin in Lauer et al's capillary zone electrophoresis because this protein has a pI value (as shown by Karger et al) within the range of pI values set forth in Table I of Lauer et al. Said human transferrin reads on the instant human biological sample.

Applicant argues that claims 1, 20, and 21 recite the need for both a buffer and an additive, and that the CHES buffer does not describe the concurrent use of an additive. Applicant argues that "[b]y use of the present invention, one can add as much additive as necessary independent of buffering capacity and the type of buffer used." However, this argument is not deemed to be persuasive because there is nothing in the instant claims that requires the buffer and additive to be different materials. The CHES buffer used by Lauer et al during its capillary zone electrophoresis has an anionic pole (from the sulfonic acid group) with a pH of more than 9 and a hydrophobic portion, from the (cyclohexylamino)ethane group. Indeed, CHES is mentioned on page 6, line 19, of the instant specification as an example of the instant additive.

With respect to Lauer et al in view of Karger et al, Applicant argues that "[i]t is not enough to merely find the missing element from a primary reference in a secondary reference and note that they might have, completely divorced from anything else, a similar property." Applicant argues that "[t]here must be a teaching, suggestion, or motivation for one using an electrophoretic device and technique such as suggested in

Lauer to look to a silicon based chromatography application and decide that, based on that completely disparate teaching, it would be obvious to attempt to separate human serum albumin using its own technique." However, this argument is not deemed to be persuasive because Lauer et al is not limited to any particular proteins. The proteins used in Lauer et al's Table I were selected so as to cover a wide range of isoelectric points and molecular weights. In the absence of anything unexpected, the selection of human transferrin for Lauer et al's capillary zone electrophoresis would have been within the skill of an artisan, particularly in view of the fact that said human transferrin has a pI value (as shown by Karger et al) within the range of pI values set forth in Table I of Lauer et al. While it is true that said human transferrin has a higher molecular weight than many of those in Lauer et al's Table I, it should be noted that Lauer et al is not limited to the protein molecular weights in said Table I. Indeed, conalbumin listed in Lauer et al's Table I and human transferrin each has a molecular weight of 77,000.

Applicant argues that:

> "Ohmura [et al] is drawn through the purification of albumin obtained by gene modification, a nonanalogous problem solved by a totally different separation process. The purified HCA in accordance with Ohmura which is to be purified from host-related substance includes only contaminants resulting from the production process which are totally different than separation from other serum-based proteins of a human biological sample. Nothing in this reference teaches or suggests electrophoresis or that its teachings may be applied to electrophoresis. Indeed, Ohmura [et al] describes adjusting the ionic strength of HAS dissolution buffing system which, if anything, when combined with Lauer teaches modifying ionic strength but not modifying charges to be associated with a particular constituent."

However, this argument is not deemed to be persuasive because Lauer et al controls the conductivity of the buffer by adding an electrolyte, such as KCl to the buffer

(see the sentence bridging pages 167 and 168). Lauer et al is not limited to KCl. It is an example of the electrolyte for controlling conductivity, i.e., controlling the ionic strength. Ohmura et al teaches that salts for adjusting ionic strength (i.e., adjusting the conductivity) include KCl and sodium sulfate (see the paragraph bridging cols. 7 and 8). It would have been obvious to one of ordinary skill in the art at the time the invention was made to have substituted the KCl in Lauer et al's buffer with sodium sulfate because the substitution of art recognized equivalent salts for adjusting ionic strength, as shown by Ohmura et al, would have been within the skill of an artisan.

Applicant argues that "Keo [et al] suggests the ability to separate hemoglobin and related proteins, not human serum proteins" and "it does not disclose the ability to separate serum proteins such as albumins and globulins." However, this argument is not deemed to be persuasive because Keo et al's clinical specimen can be a human biological liquid such as serum, plasma, cerebrospinal fluid, urine, etc (see col. 6, lines 17-22). These biological liquids, and in particular, the serum and plasma, inherently contain the instant albumin, α_1-globulin, α_2-globulin, β-globulin, β_1-globulin, β_2-globulin, and γ-globulin. In claim 1, the recited process step is "introducing" the human biological sample to the column, while in claims 20 and 21, the recited process step is one of "passing" the sample into the column. Keo et al introduces its sample into its column and passes its sample through its column (see, the examples at columns 7-9).

Applicant argues that nothing in Keo et al "appears to teach the additives as currently claimed including the recited linear alkyl sulphonates. However, this argument is not deemed to be persuasive because Keo et al's CAPS, i.e., 3-cyclohecylamino-1-

propanesulfonic acid reads on the instant zwitterionic biological buffer and additive. The claims rejected over Keo et al are silent concerning linear alkyl sulphonate.

Applicant provides arguments that Keo et al does not use of a buffering system that comprises both a buffering agent "and a material which is, by design, added at added in sufficient quantity to allow it to associate with a particular constituent of human serum and aid in separation." However, this argument is not deemed to be persuasive because Keo et al's CAPS, i.e., 3-cyclohecylamino-1-propanesulfonic acid reads on the instant zwitterionic biological buffer and additive. Indeed, CAPS is taught in the specification as being an example of the instant additive (see page 6, lines 17-20). The buffer system can further contain borate, which also reads on the instant buffer (see col. 8, lines 32-34). Serum and plasma, which are taught by Keo et al as being examples of the human biological samples that can be used (see col. 6, lines 17-22), inherently contain the instant albumin, α_1-globulin, α_2-globulin, β-globulin, β_1-globulin, β_2-globulin, and γ-globulin. It is the Examiner's position that said CAPS buffer has a hydrophobic interaction with the albumin, α_1-globulin, α_2-globulin, β-globulin, β_1-globulin, β_2-globulin, and γ-globulin and provides these proteins with at least one negative charge thereby modifying the electrophoretic mobility, as per instant claim 1. It is the Examiner's position that said CAPS has the characteristic of having a hydrophobic interaction with human albumin, as in claim 21. Furthermore, it is the Examiner's position that said CAPS has a anionic pole with a pH or more than 9 and a hydrophobic portion, as in instant claim 21.

Applicant argues that:

> "Moreover, it is well-known in the industry that capillary electrophoresis is a highly discriminating and highly specific technique. The fact that capillary electrophoresis process is so highly sensitive in terms of separating a particular constituent is of little guidance or assurance of the ability to separate others. The biological materials to be separated in accordance with the present invention are indeed different from those suggested in Keo [et al] and those of ordinary skill in the art would find this to be highly significant in terms of considering whether or not Keo's teaching would be broadly applicable to the claimed invention."

However, this argument is not deemed to be persuasive because claim 1 is silent concerning separation. Claims 20 and 21 do not recite positive separation steps, but rather, the only step recited in these claims is "passing" the recited protein constituent into the capillary. Claims 20 and 21 do recite "A method for separating" and "A method of separation" in the preamble, but there is never any positively recited separation in the process step. In claim 21 as now written, the at least one protein constituent that the method is for separating does not have to be the albumin, α_1-globulin, α_2-globulin, β-globulin, β_1-globulin, β_2-globulin, or γ-globulin. In other words, in claim 21, the albumin, α_1-globulin, α_2-globulin, β-globulin, β_1-globulin, β_2-globulin, or γ-globulin has to present in the human biological sample, but it does not have to be the at least one protein constituent that is separated. In any event, with respect to each of claims 1, 20, and 21, the glucosylated protein, such as glycolated hemoglobin, is separated by Keo et al's electrophoresis from any other proteins in the sample (see col. 3, lines 57-63). As noted above, serum and plasma, which are taught by Keo et al as being examples of the human biological samples that can be used (see col. 6, lines 17-22), inherently contain the instant albumin, α_1-globulin, α_2-globulin, β-globulin, β_1-globulin, β_2-globulin, and γ-globulin. Thus, the albumin, α_1-globulin, α_2-globulin, β-globulin, β_1-globulin, β_2-globulin, and γ-globulin are separated from the glucosylated protein.

Applicant argues that in Keo et al borate is used as a complexant, and that in the instant invention, borates, if used, are used as a buffer. However, this argument is not deemed to be persuasive because borate is used by Keo et al as a buffer (see col. 5, lines 43-65). Whether or not the borate is also a complexant is of no moment, particularly in view of the "comprising" language of the instant claims. The instant claims are open-ended and permit the presence of borate.

With respect to Ogawa et al, Applicant argues that "it is clear from the claims themselves as well as the complete disclosure of the invention that the formulation's buffering systems of the present invention are solutions." Applicant argues that "[t]hey are not gels and do not contain gelling agents." However, this argument is not deemed to be persuasive because Ogawa et al's aqueous gel-forming solution, prior to polymerization, renders obvious the instant solution and contains water (instant liquid support), buffer, and dodecyl sulfate (instant additive).

With respect to Bellon et al in view of Keyes and Bloebaum et al, Applicant argues that "the fact that the Patent Office must rely on three separate references to reject these claims, speaks volumes as to whether or not they are indeed obvious." However, this argument is not deemed to be persuasive because, for example, reliance on multiple references in a rejection does not, without more, weigh against the obviousness of the claimed invention. In re Gorman, 933 F.2d 982, 18 USPQ2d 1885 (Fed. Cir. 1991) (Court affirmed a rejection based on thirteen prior art references.).

Applicant argues that TRIS buffer described by Bellon et al has a pH between 6.6 and 8.8. Applicant argues that Bellon et al fails to teach the pH range of the composition of the present invention. However, this argument is not deemed to be persuasive because the claimed pH range of between 9 and 11 is met by Bellon et al's disclosure of a pH of about 9 (see col. 5, line 43).

Applicant argues that Bloebaum et al concerns conforming various solutions to normal physiology, Keyes concerns modification of proteins, and that there is no reason to combine Bellon et al with Bloebaum et al and Keyes. However, this argument is not deemed to be persuasive because Keyes (col. 17, lines 39-40 and 49) and Bloebaum et al (col. 6, line 33) have been relied upon by the Examiner for showing what is very well known, i.e., that Tris can buffer at pH 9.1. The Examiner maintains that it would have been obvious to one of ordinary skill in the art at the time the invention was made to have prepared Bellon et al's buffer solution at a pH of about 9, such as 9.1 because Tris can buffer at such a pH, as shown by Keyes and Bloebaum et al, and Bellon et al teaches a pH of about 9, as noted above.

Conclusion

23. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alan Diamond whose telephone number is 571-272-1338. The examiner can normally be reached on Monday through Friday, 5:30 a.m. to 2:00 p.m. ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen can be reached on 571-272-1342. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Alan Diamond
Primary Examiner
Art Unit 1753

Alan Diamond
December 29, 2005